Infectious Retina
Raman Bhakhri, OD, FAAO
Assistant Professor
SCCO/MKU

Disclosure Statement:
Nothing to disclose

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Common Posterior Segment Manifestations
- HIV Retinopathy
- Cytomegalovirus (CMV)
- Acute Retinal Necrosis (ARN)
- Progressive Outer Retinal Necrosis (PORN)
- Tuberculosis (TB)
- Toxoplasmosis
- Syphilis
- Cat Scratch Disease

The Fight Against AIDS
- Dr. Thomas R. Frieden, the director of the Centers for Disease Control and Prevention, and Dr. Jonathan Mermin, the agency’s chief of AIDS prevention, paint a bleak picture of the fight.
  - “Hundreds of thousands of people with diagnosed H.I.V. infection are not receiving care or antiretroviral treatment,” they wrote. “These people account for most new H.I.V. transmission.”
- Nearly 65 percent of the estimated 1.2 million Americans with H.I.V. are not on treatment; many disappear right after being tested.
- Proposed budget cuts to PEPFAR (Presidents Emergency Plan for AIDS Relief)

HAART
- Highly Active Antiretroviral therapy (HAART) is the combination of several antiretroviral medicines used to slow the rate at which HIV multiplies in the body.
- The use of three or more antiretroviral medicines-sometimes referred to as an anti-HIV “cocktail”—is currently the standard treatment for H.I.V. infection
  - Nucleoside/nucleotide reverse transcriptase inhibitors
  - Nonnucleoside reverse transcriptase inhibitors
  - Protease inhibitors
  - Entry inhibitors
  - Integrase inhibitors
**HIV Retinopathy**

- Retinal Microvasculopathy
  - Use to occur in 50-70% of patients
- Symptoms: none
- Characterized by:
  - dot blot hemorrhages
  - cotton wool spots
  - Roth spots
  - retinal microaneurysms
- Prevalence lowered by advent of HAART
- Thought to be due to increased plasma viscosity, immune complex deposits, and direct cytopathic effect of the virus on the blood vessel endothelial layer.

**Control viral load undetectable**
- Most findings resolve with time.
- Can be confused with diabetic retinopathy or hypertensive retinopathy.

**Cytomegalovirus (CMV)**

- Most common cause of intraocular infection in patients with AIDS.
  - Part of the herpes family of viruses
  - CMV spreads from person to person through body fluids, such as blood, saliva, urine, semen, and breast milk
  - Seen in patients with a CD4 count less than 50 cells/μL
  - Represents re-activation of latent CMV infection
  - Necrosis through direct cell destruction, release of viral products from infected cells, and production of inflammatory molecules such as cytokines by virus infected and/or nearby cells

**Signs and Symptoms**

- Symptoms:
  - Floaters
  - Photopsias
  - Decreased vision
  - Minimal a/c reaction
- Signs:
  - Necrotising retinitis (cheese)
  - Hemorrhages (ketchup)
  - Vascular sheathing
  - Uveitis
  - Retinal detachment

**Cytomegalovirus (CMV)**

- Types:
  - Fulminant: Large areas of necrosis with hemes found within the arcades
  - Indolent: Retinal atrophy with minimal hemes in the periphery
  - Perivascular: frosted appearance
- Progression can lead to papillitis, macular edema, retinal detachment
  - Slow course, 250 um per week
CMV Treatment Options

- IV ganciclovir, cidofovir, foscarnet
  - Individually or in combination
- Oral ganciclovir or valganciclovir
- Intravitreal ganciclovir and foscarnet
- Ganciclovir implant
  - Systemic toxicity
  - Better efficacy against CMV in the implanted eye
  - No indwelling catheter
  - Useful if patient is intolerant of systemic ganciclovir or if progression continues despite intravenous treatment

Acute Retinal Necrosis (ARN)

- Necrotizing retinitis that presents with:
  - Varicella zoster virus (VZV)-more severe presentation
  - Herpes Simplex Virus (HSV)
  - Cytomegalovirus (CMV) (rare)
- Can occur in immunocompetent or immunocompromised patients

Signs and symptoms

- Symptoms:
  - Eye pain, photophobia
  - Decreased vision
  - Floaters
- Signs:
  - Necrotic lesions in periphery (with rapid progression)
  - Hemorrhaging (minor)
  - Retinitis/Vitritis/Uveitis
  - Disc edema
  - Retinal detachment
Acute Retinal Necrosis

- IV acyclovir/valacyclovir/famciclovir in conjunction with oral
- For anterior segment inflammation:
  - Cycloplegic with topical steroid
  - Barricade laser
  - Relapse is common, initiate initial therapy
  - Systemic steroids??
    - Virectomy? Release of traction

Progressive outer retinal necrosis (PORN)

- Caused by the varicella-zoster virus
  - Double stranded DNA virus of the herpes group
  - Virus is spread through direct contact with the rash or by sneezing, coughing, and breathing
  - Virus remains latent in sensory ganglia
    - Reactivated during times of loss of T cell regulatory control (AIDS)
  - Necrosis through direct cell destruction, release of viral products from infected cells, and production of inflammatory molecules such as cytokines by virus infected and/or nearby cells

PORN

- Facial rash/scars: Patients had an episode of cutaneous zoster a mean of two months before onset of visual symptoms.
- Minimal intraocular inflammation CD4 count less than 21 in most studies
- Bilateral retinal necrosis involving the outer retinal layers with relative sparing of the inner retina and retinal vasculature.
- Lesions progress, and become confluent and full-thickness

- Optic nerve involvement: edema, hyperemia, atrophy (17%)
- Rhegmatogenous retinal detachment secondary to atrophic, thin retina with multiple holes (70%)
  - Number one cause of vision loss
Progressive Outer Retinal Necrosis

- Various combinations of IV, oral, and intravitreal antivirals. Ganciclovir, acyclovir, foscarnet
- Barricade laser
- Highly active antiretroviral therapy (HAART)

**PORN Treatment Options:**

<table>
<thead>
<tr>
<th></th>
<th>PORN</th>
<th>ARN</th>
<th>CMV</th>
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</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>Floaters, VA loss, peripheral constriction, no pain</td>
<td>Heavy vision, peripheral constriction, pain</td>
<td>Mild or no change in VA, constricted fields, floaters, no pain</td>
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<tr>
<td><strong>Progression</strong></td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Optic Nerve Involvement</strong></td>
<td>Possible</td>
<td>Possible</td>
<td>Possible</td>
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<tr>
<td><strong>Etiology</strong></td>
<td>VZV</td>
<td>VZV, HSV1,2</td>
<td>CMV</td>
</tr>
<tr>
<td><strong>Inflammation</strong></td>
<td>Minimal or none</td>
<td>Vitreal and/or AC</td>
<td>Ac and ant, vitreous</td>
</tr>
<tr>
<td><strong>Vascular Inflammation</strong></td>
<td>None</td>
<td>Vasculitis</td>
<td>Vasculitis</td>
</tr>
<tr>
<td><strong>HIV/AIDS</strong></td>
<td>+</td>
<td>+ or -</td>
<td>+</td>
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**Differentiating the Herpetic Retinopathies**
Tuberculosis

- Caused by airborne transmission and infection with *Mycobacterium tuberculosis*, with main infection at the lungs
- Cause of nearly 3 million deaths per year.
- Risk of tuberculosis higher in patients who are immune-compromised.
  
  The risk of developing tuberculosis (TB) is estimated to be between 20-37 times greater in people living with HIV than among those without HIV infection.
  
  2010: 8.8 million new cases of TB, of which 1.1 million were among people living with HIV.

Skid row outbreak
Rising Drug Costs

Additional Testing
- Mantoux test: hardening of less than 15 is normal
- TB blood tests (also called interferon-gamma release assays or IGRAas):
  - Quanferon TB Gold: measure interferon released by sensitized T-cells, more specific
  - T-SPOT
- Chest X-Rays

Symptoms:
- Pain, decreased vision, floaters

Signs:
- Choroiditis
- Subretinal abscess, subretinitis, and tuberculomas
- Vitritis
- Rare: Retinal involvement-vasculitis

Most commonly affects the choroid, due to high oxygen content and vascularization.

Fundus findings in tuberculosis can be divided into four groups:
- Choroidal tubercules:
  - Small inflammatory nodule that forms when the immune system builds a wall around the TB
- Choroidal tuberculoma:
  - Tubercules continue to grow into a larger mass
- Subretinal abscess-necrotizing granulomas
- Serpiginous like choroiditis

**Tuberculosis**

- Treatment:
  - RIPE: Rifampin, Isoniazid, Pyrazinamide, Ethambutol for 4-6 months
  - Steroids can be used to control inflammation but only in conjunction with anti-bacterials

**Toxoplasmosis**

- Due to Toxoplasma gondii, protozoan parasite, which is transmitted by ingesting contaminated water and food (raw meats, raw eggs, unpasteurized milk), exposure to cats
  - Two Types:
    - Acquired
    - Congenital
  - Most common cause of posterior uveitis in any patient.
  - Testing:
    - Toxoplasmosis antibody titer
    - PCR

**Pathophysiology**

- Tachyzoite: active proliferating form: destructive immune response.
  - Under pressure of the immune system, tachyzoites differentiate into bradyzoites, forming tissue cysts.
  - Latent form, may persist indefinitely in host tissues. Refractory to most currently available antiparasitic drugs
  - Chronic T. gondii infection cannot be cured.

**Toxoplasmosis**

- Symptoms:
  - Decreased vision
  - Floaters
  - Pain, if anterior chamber reaction
- Signs:
  - Necrotizing retinitis
  - Vasculitis
  - Viritis (reduced compared to immunocompetent pt)
  - Adjacent retinocochoroidal scars not seen, suggesting that these represent recently acquired infections
  - High association with CNS disease, MRI indicated

**Acquired toxoplasmosis**

- Due to Toxoplasma gondii, protozoan parasite, which is transmitted by ingesting contaminated water and food (raw meats, raw eggs, unpasteurized milk), exposure to cats
  - Two Types:
    - Acquired
    - Congenital
  - Most common cause of posterior uveitis in any patient.
  - Testing:
    - Toxoplasmosis antibody titer
    - PCR
Treatment

- Main Factors Influencing Treatment Decision on Active Toxoplasmic Retinochoroiditis
  - Immune status of the individual
  - Location and size of the active lesion
  - Presence of macular and/or optic disc edema
  - Degree of vitritis and of decreased vision
  - Special situations (newborns, pregnant women, drug allergy)
  - Adverse effects of antiparasitic drugs and corticosteroids

Toxoplasmosis Treatment:

- Pyrimethamine and either sulfadiazine or clindamycin in standard dosages with oral pred 24 hrs after antibiotics begin
- Trimethoprim/sulfamethoxazole: reoccurrences
- Folinic acid to minimize bone marrow toxicity
- Anterior chamber reaction: cycloplegic and steroid

Syphilis

- Syphilis is a chronic venereal disease caused by the spirochete Treponema pallidum.
- In the United States, the rates of syphilis have been increasing since 2000, particularly in HIV-positive patients and homosexual men.
- The Great Masquerader……
Syphilis Staging

- **Primary syphilis:**
  - Painless chancre that develops at the site of infection an average of three weeks after exposure.

- **Secondary syphilis:**
  - The most common features are fever, lymphadenopathy, diffuse rash, and genital or perineal condyloma lata.

- **Latent stage:**
  - Patients are asymptomatic. Serologic tests are positive for *T. pallidum*.

- **Tertiary:**
  - Infection can involve any organ system.

Types

- **Two Types:**
  - Acquired
  - Congenital
    - Widely spaced, centrally notched anterior incisors (Hutchinson’s teeth) and the abnormal facies (saddle nose). Congenital syphilis may present with interstitial keratitis, uveitis, optic neuritis, glaucoma, cataract, and/or retinal vasculitis.
    - Hutchinson Triad: deafness, Hutchinson’s teeth, interstitial keratitis.

- **Two Types of antibody tests:** non-treponemal and treponemal
  - Non-treponemal: RPR & VDRL detect antibodies directed against host antigens. Advantages of quantifiability reflect both disease activity and response to therapy, and can be used to test for reinfection. Limited sensitivity—has been suggested to be as low as 70 percent.
  - Treponemal: FTA-ABS & MHA-TP tests measure serum antibodies directed specifically against the *T. Pallidum* and are highly sensitive.
    - Not reliable in gauging response to treatment.
    - False positive with collagen vascular disease, advanced age and HIV infection.
    - Positive for life even despite treatment.

Syphilis

- **Symptoms:**
  - Decreased vision
  - Floaters
  - Pain
  - Photophobia

- **Signs:** (no sign is pathognomonic)
  - Uveitis—strong predictor of HIV co-infection
  - Optic neuritis
  - Retinitis
  - Choroiditis
  - Vasculitis
    - Most common finding in one study was panuveitis with retinitis
Patients with ocular syphilis should undergo CSF testing and, regardless of findings, be treated as neurosyphilis with 10 to 14 days of high-dose intravenous followed by three weekly injections of IM penicillin. Allergy: tetracycline or doxycycline.

Uveitis: cycloplegics with topical steroids.

**Cat Scratch Disease**

- **Cause:** Bartonella henselae

- **Etiology and Pathology:**
  - Fleas (Ctenocephalides felis) carry B. henselae and can transmit the bacterium from cat to cat.
  - Exposure to kittens is a greater risk factor than exposure to adult cats.
  - B. henselae can be transmitted to humans following contact with cats (scratches, bites) and possibly following contact with cat fleas.

- 22,000 cases yearly in the U.S. (about 6.6 cases per 100,000)

- No racial nor gender predilection

- Majority of cases are in pediatric patients with cat contacts.

**Treatment Options**

- IV Penicillin

- Patients with ocular syphilis should undergo CSF testing and, regardless of findings, be treated as neurosyphilis with 10 to 14 days of high-dose intravenous followed by three weekly injections of IM penicillin. Allergy: tetracycline or doxycycline.

- Uveitis: cycloplegics with topical steroids.
Cat Scratch Disease

Testing:
- Indirect fluorescent assay specific for antibodies directed against B. henselae.
  - This test has a sensitivity and specificity above 90 percent
- Enzyme-linked immunoassay for both IgG and IgM anti-B. henselae antibodies.
- PCR-based techniques
  - Very sensitive and can differentiate between Bartonella species
  - Harder to obtain

Signs:
- granulomatous conjunctivitis with preauricular lymphadenopathy
- systemic lymphadenopathy
- optic nerve edema
- subretinal fluid, exudates, or a macular star
- focal chorioretinitis
- positive skin test or serum titer for Bartonella H.

Symptoms:
- systemic symptoms of disease may resemble a flu-like illness (malaise/weakness, low-grade fever, headache, and joint or muscle pains)
- patients may also notice enlarged regional lymph nodes in the axilla, groin, neck, or head
- decreased/blurry vision, usually in one eye
- red eye
- patients may notice decreased visual field
Treatment:

- Controversial
- Documented that patients will almost always get better on their own; final visual acuity is 20/40 or better in 93% of patients
- Treatments include doxycycline, erythromycin, rifampin, azithromycin, ciprofloxacin